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Chromosome 22q11.2 Deletion in a Boy With Opitz (G/BBB) Syndrome

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This report is on a 14-month-old boy with manifestations of Opitz (G/BBB) syndrome in whom a 22q11.2 deletion was found. Deletion analysis was requested because of some findings in this patient reminiscent of velocardiofacial (VCF) syndrome. The extent of aspiration and of respiratory symptoms in this child is not usually seen in VCF syndrome. Opitz syndrome maps to at least two loci, one on Xp, the other on 22q11.2.

KEY WORDS: chromosome 22q11.2 deletion, Opitz syndrome, G/BBB syndrome, velocardiofacial syndrome

INTRODUCTION

Opitz (G/BBB) syndrome (OS) is an autosomal-dominant multiple congenital anomaly (MCA) syndrome, often more severe in males [Opitz et al., 1969a,b; Opitz, 1987]. Affected males have hypospadias, telecanthus/hypertelorism, and other midline abnormalities, often involving laryngotracheoesophageal (LTE) structures [Brooks et al., 1992]. The morbidity and mortality associated with OS are often attributed to the LTE anomalies. We report on a boy, age 14 months, with physical characteristics of OS and a 22q11.2 deletion.

CLINICAL REPORT

The patient was a 3,150-g boy, the product of a 37-week gestation delivered by cesarean section for failing to progress to a 23-year-old $G_2P_0SAB_1$ white woman with an otherwise unremarkable pregnancy history. Early during infancy the baby developed gastroesophageal reflux (GER), with respiratory distress necessitating use of bronchodilator drugs. Over the following months he reportedly had recurrent episodes of choking and presumed aspiration. These were considered suggestive of neuromuscular dysfunction, since esophagoscopy documented a Zenker diverticulum, but no other structural LTE abnormalities. Several barium swallow studies noted no evidence of aspiration, but did show continuous nasopharyngeal regurgitation. He had numerous hospitalizations related to this problem, and recently during one such hospitalization we were asked to evaluate him because of unusual appearance.

At age 14 months his weight and length were at the 25th centile, and his OFC (45.5 cm) was at the 10th centile. He had (Fig. 1) a prominent metopic ridge, "cupped" ears, downslanted palpebral fissures, flat philtrum, broad and low nasal bridge, telecanthus, and small chin. His palatal musculature was unusual in that the muscles ran lengthwise, but his uvula was not bifid. Physical findings were otherwise normal, except for grade I hypospadias and a slightly hypoplastic scrotum. Renal ultrasound and echocardiography findings

Fig. 1. Face. Note prominent metopic ridge, "cup-shaped" ears, broad nasal bridge, downslanted palpebral fissures.

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were normal. Neurodevelopmental status was normal, except for delays in expressive language with normal receptive skills.

Prophase chromosomes were normal. A FISH analysis with DiGeorge probe (Oncor, Inc., Gaithersburg, MD) was requested on the basis of his unusual palatal findings and some of his facial traits. FISH analysis showed a lack of signal on one of the 22 chromosomes consistent with a deletion in the 22q11.2 band (Fig. 2). The father has been unavailable for study, but the mother's chromosomes were normal, with no evidence of chromosome 22 deletion with the DiGeorge probe. The family history was noncontributory.

DISCUSSION

Opitz syndrome (OS) is a heterogeneous condition considered X-linked in some cases [Christian et al., 1969; Opitz et al., 1969a,b; Stevens and Wilroy, 1988; Verloes et al., in press], autosomal in others [Côté et al., 1981; Farndon and Donnai, 1983; Opitz, 1987; Urioste et al., in press]. McDonald-McGinn et al. [in press] report on a family with autosomal-dominant paternally-inherited OS, as well as on two additional cases of OS, all with 22q11.2 deletions. Our patient is the fifth to be identified with OS and a 22q11.2 deletion, suggesting that in a subset of patients OS may result from a 22q11.2 deletion. In addition, these cases suggest that the phenotype associated with 22q11.2 microdeletions should be expanded to include features of OS, in addition to those previously reported including VCFS, DiGeorge syndrome, and conotruncal anomaly face syndrome [Burn et al., 1993].

Fig. 2. Representative metaphase demonstrating lack of signal on one of the number 22 chromosomes. Chromosome 22 with normal signal pattern is indicated by solid arrow. Deleted chromosome 22 with distal q arm marker present but without DiGeorge probe signal is indicated by open arrow.

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